CHAPTER 46
Miscellaneous Heart Murmurs

KEY TEACHING POINTS

- Some miscellaneous murmurs are so distinctive that the *presence* of the characteristic murmur is diagnostic: this is true for mitral valve prolapse, tricuspid regurgitation, and pulmonic regurgitation.
- Abnormalities of the precordial pulsation and neck veins—including the "right ventricular rock," lower sternal pulsation, pulsatile liver, and CV venous waveform—greatly increase the probability of tricuspid regurgitation.
- The murmurs of hypertrophic cardiomyopathy and mitral valve prolapse respond to the Valsalva strain and squatting-to-standing maneuvers in a diagnostic fashion. Both of these maneuvers alter venous return.
- Hemodialysis fistulas frequently produce systolic remnants of sound near the upper sternum, sounds easily mistaken for cardiac murmurs unless the entire arm (and fistula) is auscultated.

HYPERTROPHIC CARDIOMYOPATHY

I. THE MURMUR

The murmur of hypertrophic cardiomyopathy is usually midsystolic, harsh in quality, and loudest at the lower left sternal border or between the lower left sternal border and apex.[1] The murmur may obliterate the second heart sound and become late systolic, especially if there is associated mitral regurgitation. The intensity of the murmur behaves in distinctive ways during maneuvers, altering venous return to the heart (see Chapter 43).

II. ASSOCIATED FINDINGS

The palpable apex beat may be sustained and the arterial pulse hyperkinetic (see Chapters 15 and 38). Although pulsus bisferiens has been described in hypertrophic cardiomyopathy,[2] this refers to a finding seen on intra-arterial pressure tracings, not a palpable one at the bedside.[3] The second heart sound is usually single or physiologically split, though in 10% splitting is paradoxic or reversed.[1] More than half of patients have audible fourth heart sounds.[1]

MITRAL REGURGITATION

I. THE FINDING

A. THE MURMUR

The murmur of chronic mitral regurgitation is usually holosystolic, high in frequency, and loudest at the apex.[4] It radiates to the axilla and inferior angle of the left scapula, although in some patients with isolated incompetence of the medial portion of the posterior leaflet, the murmur radiates instead to the right base and even into the neck, thus mimicking aortic stenosis.[4,5]

In 1832 James Hope was the first to describe the apical systolic murmur of mitral regurgitation.[4,6]

B. ASSOCIATED FINDINGS

In chronic mitral regurgitation the intensity of S_1 is normal 75% of the time, loud 12% of the time, and soft 12% of the time. In 50% of patients, S_2 splitting is wide and physiologic.[4] An associated S_3 is common, appearing in 89% with severe regurgitation. S_4 is rare.

Associated cardiac findings are an enlarged, laterally displaced palpable apical movement,[7] a palpable lower parasternal movement from an enlarged left atrium or associated tricuspid regurgitation (see Chapter 38),[8] and in younger patients a hyperkinetic arterial pulse (see Chapter 15).[9] Neck veins are normal unless the patient has decompensated heart failure.

II. CLINICAL SIGNIFICANCE

A. DETECTING MITRAL REGURGITATION

The presence of the characteristic murmur of mitral regurgitation increases the probability that regurgitation is present, at least to a mild degree (LR = 5.4; see Chapter 43). Although 25% to 50% of patients with *mild* regurgitation lack a murmur, the absence of the characteristic murmur decreases the probability of *moderate-to-severe* mitral regurgitation (LR = 0.3, see Chapter 43).

B. SEVERITY OF MITRAL REGURGITATION

1. THE MURMUR

In a very general way the intensity of the murmur of mitral regurgitation correlates with the severity of regurgitation, especially for rheumatic mitral regurgitation ($r = 0.67$), but less so for ischemic or functional* mitral regurgitation ($r = 0.45$).[10-12] A mitral regurgitation murmur of grade 3 intensity or louder increases the probability of moderate-to-severe regurgitation (LR = 4.4; EBM Box 46.1).

2. OTHER FINDINGS

Patients with severe mitral regurgitation may have a late systolic sustained left lower parasternal impulse from a dilated left atrium (Chapter 38 discusses how

*Functional mitral regurgitation implies that the primary problem is cardiomyopathy, which dilates the atrioventricular ring and renders the valve incompetent. Because of their low ejection fraction, these patients often do not tolerate valve replacement.

to distinguish this impulse from a right ventricular impulse or atrial impulse). The degree of this movement correlates well with severity of regurgitation (r = 0.93, $p < 0.01$), as long as the patient does not have associated mitral stenosis (the presence of mitral stenosis confounds analyzing the parasternal impulse of patients with mitral regurgitation because the impulse could represent either a large left atrium from severe regurgitation or a hypertensive right ventricle from mitral stenosis).[8,17]

Some studies correlate the third heart sound with severity of mitral regurgitation,[14] whereas others do not.[13] Overall, the pooled LR is not significant (see EBM Box 46.1).

C. DISTINGUISHING ACUTE FROM CHRONIC MITRAL REGURGITATION

The physical signs of acute and chronic mitral regurgitation differ in several ways. In acute lesions, patients are acutely ill with elevated neck veins and signs of pulmonary edema; in chronic lesions, these signs may be absent. In acute

EBM BOX 46.1
*Severity of Mitral and Tricuspid Regurgitation**

Finding (Reference)†	*Sensitivity (%)*	*Specificity (%)*	Likelihood Ratio‡ if Finding is	
			Present	*Absent*
Detecting Moderate-to-Severe Mitral Regurgitation (In Patients With the Characteristic Murmur)				
Murmur grade 3 or louder[12]	85	81	**4.4**	**0.2**
S_3 gallop[13,14]	24-41	77-98	NS	0.8
Detecting Moderate-to-Severe Tricuspid Regurgitation				
Inspection of Neck Veins				
Early systolic outward movement (CV wave)[15]	37	97	**10.9**	0.7
Precordial and Hepatic Pulsations				
Lower sternal precordial pulsations[15]	17	99	**12.5**	0.8
RV rock[15]	5	100	**31.4**	NS
Pulsatile liver[15,16]	12-30	92-99	**6.5**	NS

*Diagnostic standard: for *moderate-to-severe mitral regurgitation,* regurgitant fraction >40% by Doppler echocardiography[12,14] or as assessed visually from echocardiography[15] or angiography;[13] for *moderate-to-severe tricuspid regurgitation*, 3+ or 4+ by angiography[16] or as assessed visually from echocardiography.[15]

†Definition of findings: for *RV rock,* see the text and Chapter 38.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, Not significant; *RV,* right ventricular.

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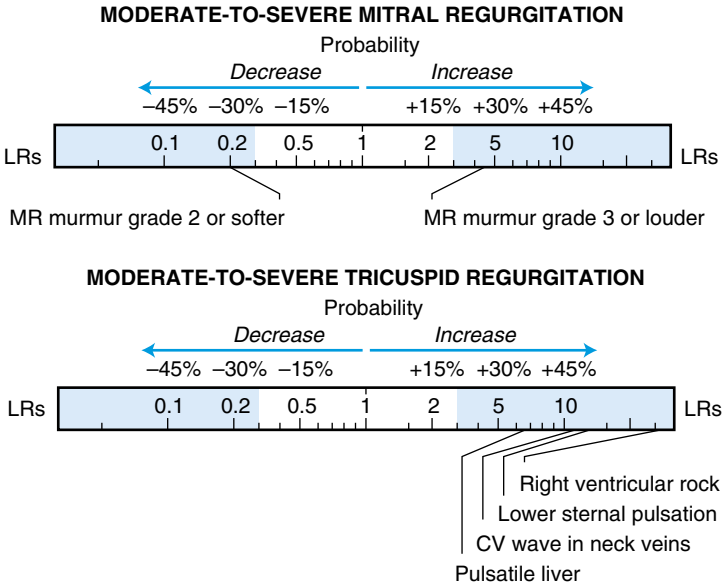

lesions the pulse is rapid and regular; in chronic lesions it is often slow and irregular (from atrial fibrillation).[18] In acute lesions the murmur may be short and confined to early systole (40% of patients in one series) because the left atrial pressure is so high it equilibrates with left ventricular pressures by mid-to-late systole and thus eliminates the regurgitation gradient;[19,20] in chronic lesions the timing varies, although holosystolic and late systolic are most common. In acute lesions the fourth heart sound is common (80% in one series); in chronic lesions the fourth heart sound is rare, either because the atrial contraction is absent (i.e., atrial fibrillation) or the atrium is so dilated it cannot contract strongly.[10,18,21]

D. PAPILLARY MUSCLE DYSFUNCTION

Papillary muscle dysfunction refers to a murmur of mitral regurgitation that develops in the setting of myocardial ischemia. The murmur, which is usually transient, may be holosystolic, midsystolic, or late systolic. It appears in up to 20% of patients with myocardial infarction,[22] in whom it is associated with a higher incidence of persistent chest pain in the intensive care unit (45% vs. 26% without murmur) and a higher 1-year mortality (18% vs. 10%).[22]

MITRAL VALVE PROLAPSE

I. INTRODUCTION

Mitral valve prolapse describes an abnormal posterosuperior movement of the mitral valve leaflets into the left atrium after they close at the beginning of

systole. It is an important cause of late systolic murmurs and mid-to-late systolic clicks,[23-25] and in developed nations it is the most common cause of mitral regurgitation.[26]

At the beginning of the 20th century, most clinicians believed late systolic murmurs were benign and late systolic clicks were generated outside of the heart.[23,24] In 1963 Barlow performed angiograms in several patients with late systolic murmurs and proved the cause was mitral prolapse and regurgitation.[27]

II. THE FINDINGS

A. THE MURMUR

The murmur of mitral valve prolapse is loudest at the apex and is sometimes musical (see Chapter 43). It is characteristically late systolic because the mitral leaflets are well supported by chordae tendineae and competent during early systole, but lose this support as the ventricle becomes smaller during late systole, allowing the leaflets to buckle backward toward the left atrium and create a regurgitant leak.[23-25]

B. THE CLICKS

The clicks of mitral valve prolapse occur during mid-to-late systole and are loudest at the apex or left lower sternal border.[23] They are sometimes multiple. In patients with both a click and a murmur, the click introduces the murmur 65% of the time and occurs just after the beginning of the murmur 35% of the time.[23] Sudden deceleration of the billowing mitral leaflet, as it prolapses into the left atrial cavity, causes the sound, which thus resembles the sound produced by a parachute or sail that suddenly tenses as it fills with wind.[28]

C. RESPONSE OF MURMURS AND CLICKS TO MANEUVERS

Bedside maneuvers that alter venous return or afterload (i.e., systemic vascular resistance) change both the timing of the clicks and murmurs and the intensity of the murmur, although they affect timing and intensity independently.

The *timing* of clicks and murmur depends on the venous return to the heart (Fig. 46.1). Reductions in venous return—by straining during the Valsalva maneuver or moving from squatting-to-standing—causes the ventricular chamber to become smaller and the mitral leaflets to prolapse earlier during systole, thus moving the click closer to S_1 and making the murmur longer.[23,25]

In contrast, the *intensity* of the murmur depends more on afterload, and in this way the response resembles that of chronic mitral regurgitation (see Chapter 43). As afterload is reduced with amyl nitrite inhalation, the murmur of mitral valve prolapse becomes fainter.[23] The Valsalva strain also usually makes the murmur *softer*. However, squatting-to-standing makes the murmur *louder*, perhaps because the standing position invokes sufficient sympathetic tone to preserve afterload, while at the same time making ventricular contractions more vigorous, thus intensifying the sound.[23†]

[†] Mitral valve prolapse is therefore an important cause of the false-positive result when using the squatting-to-standing maneuver to diagnose obstructive cardiomyopathy (see Chapter 43).

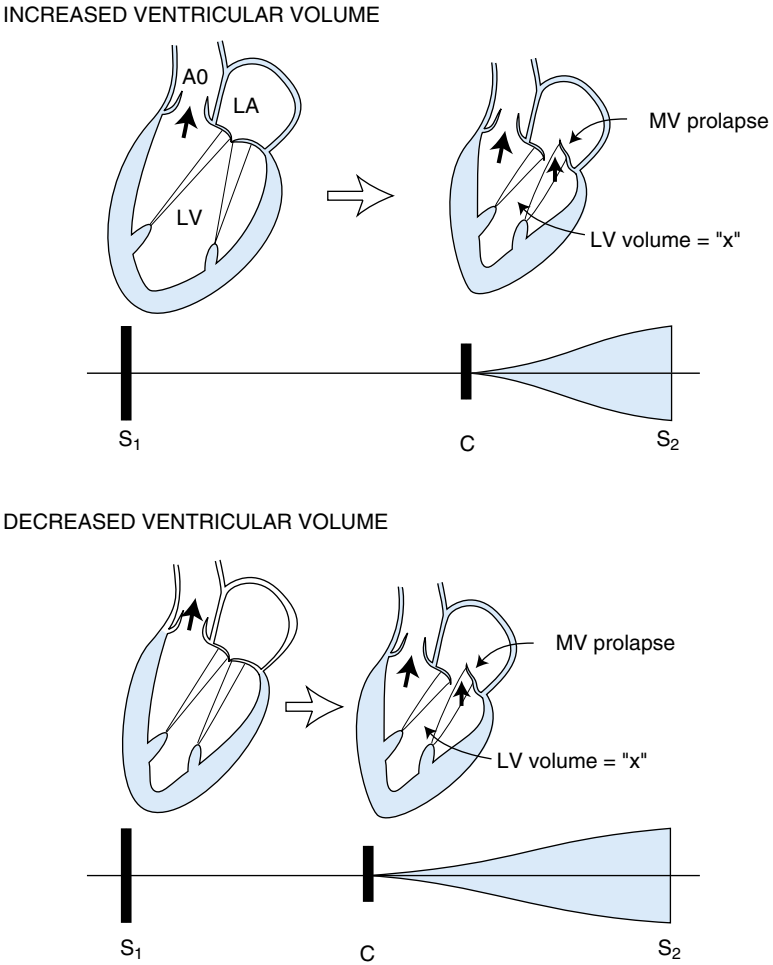

FIG. 46.1 TIMING OF MITRAL VALVE PROLAPSE. In each example, the left ventricle is ejecting blood during systole and prolapse of the mitral valve occurs at the moment ventricular volume = "x." If ventricular systole begins with a relatively large ventricular volume (*top row*), the ventricular volume of "x" is delayed until late systole. If ventricular systole instead begins with a smaller ventricular volume (e.g., by straining during the Valsalva maneuver or moving from squatting-to-standing, *bottom row*), the ventricular volume of "x" is reached earlier during systole, causing the click and murmur to move toward S_1. *AO*, Aorta; *C*, click; *LA*, left atrium; *LV*, left ventricle; *MV*, mitral valve.

III. CLINICAL SIGNIFICANCE

A. DETECTION OF MITRAL VALVE PROLAPSE

The presence of the characteristic click and murmur of mitral valve prolapse increases greatly the probability of prolapse, as detected by echocardiography (LR = 12.1; see Chapter 43). Indeed, some have argued that the auscultatory

criteria alone are sufficient for diagnosis.[29,30] The criteria for diagnosing mitral valve prolapse are the reproducible finding in a young patient of a mid-to-late systolic click or late systolic murmur at or near the apex. These sounds should shift their timing with respect to S_1 and S_2 in response to the Valsalva and squatting-to-standing maneuvers (see the section on Response of Murmurs and Clicks to Maneuvers and Fig. 46.1). These criteria require the patient to be young to avoid confusion with papillary muscle dysfunction, a common cause of late systolic murmurs in older patients.[29] The click should be mobile and occur in mid-to-late systole to eliminate confusion with other short systolic sounds, such as the split S_1 and aortic ejection sound (Chapters 41 and 42 further differentiate these sounds).[29,30]

B. RISK OF SIGNIFICANT MITRAL REGURGITATION

The risk of significant mitral regurgitation in mitral valve prolapse is low. In one study of 291 patients with a click or murmur presenting to a cardiologist (which biases selection toward more severe cases), none of the patients with an isolated click developed significant mitral regurgitation over 8 years of follow-up, and only 3% of those with murmurs required mitral valve replacement.[31]

TRICUSPID REGURGITATION

I. THE FINDINGS

The physical findings of tricuspid regurgitation depend on the patient's pulmonary pressure, which may be high (high-pressure tricuspid regurgitation) or normal (low-pressure tricuspid regurgitation). **High-pressure tricuspid regurgitation** is commonly due to left-sided heart disease; **low-pressure tricuspid regurgitation** commonly results from endocarditis of the tricuspid valve.

A. THE MURMUR

Whether pulmonary pressures are high or low, the murmur of tricuspid regurgitation is typically loudest at the lower left sternal border, becomes louder during inspiration, and may radiate below the xiphoid process.[32]

1. HIGH-PRESSURE TRICUSPID REGURGITATION

The murmur of high-pressure tricuspid regurgitation is holosystolic because the elevated right ventricular pressures exceed right atrial pressures throughout systole. The murmur becomes louder during inspiration (**Carvallo sign**) in 75% of patients and during manual pressure over the liver in 60% of patients.[16,33-37]

In some patients with high-pressure tricuspid regurgitation, the murmur is loudest at the apex because the enlarged right ventricle has replaced the normal position of the left ventricle. At this location, the resulting holosystolic apical murmur resembles mitral regurgitation, which in the 1950s led to the significant bedside error of misdiagnosing mitral regurgitation in some patients with mitral stenosis, thus inappropriately denying them valvuloplasty (a procedure contraindicated with severe mitral regurgitation).[38] Clues that help the clinician to correctly recognize the apical holosystolic murmur as tricuspid regurgitation are the associated findings of an identical murmur at the lower sternal border, inspiratory augmentation of the murmur, elevated neck veins, and pulsatile liver.[38]

2. LOW-PRESSURE TRICUSPID REGURGITATION

If pulmonary and right ventricular pressures are normal, the murmur of tricuspid regurgitation is confined to early systole, because right atrial and right ventricular pressures equilibrate by mid systole, thus eliminating the gradient causing the murmur.[39]

B. OTHER FINDINGS

1. HIGH-PRESSURE TRICUSPID REGURGITATION

Other important cardiac findings are elevated neck veins (more than 90% of patients), a systolic regurgitant wave in the neck veins (51% to 83% of patients), and systolic retraction of the apical impulse (22% of patients).[16,34,36] Thirty percent to 91% of patients have a pulsatile liver, and 90% have edema, ascites, or both.[16,32,34,36] In some patients there is an outward precordial pulsation of the lower sternum (from ejection of blood into the right atrium and liver). This sternal movement, when combined with simultaneous apical retraction (from right ventricular contraction), creates a distinctive rocking motion (i.e., apex moves in and lower sternum out at the same time), a motion called **right ventricular rock** (see Chapter 38).[15]

2. LOW-PRESSURE TRICUSPID REGURGITATION

In these patients the neck veins and apical impulse are normal, and there is no edema, pulsatile liver, or ascites.

C. ESTIMATING VENOUS PRESSURE IN TRICUSPID REGURGITATION

Estimates of venous pressure are useful because they indicate right ventricular *diastolic* pressures (or filling pressures), which provides important clues to the etiology of ascites and edema (see Chapter 36). However, in tricuspid regurgitation the neck veins characteristically reveal a large *systolic* wave, raising the question of whether bedside estimates of venous pressure still reliably indicate the right heart filling pressures.

In patients with tricuspid regurgitation (and no tricuspid stenosis), catheter measurements of the *mean* pressure in the right atrium correlate closely with right ventricular end-diastolic pressure ($r = 0.94$, $p < 0.001$, slope 1).[34] Mean atrial pressure is estimated at the bedside by identifying which patient position brings out the regurgitant waves. If the regurgitant waves are visible when the patient is supine, then venous diastolic pressure must be low (i.e., the waves collapse and become visible because the diastolic venous pressure is below the level of the sternum, or low). The mean atrial pressure (i.e., central venous pressure) in these patients is probably normal. On the other hand, if the regurgitant waves are only visible in the upright position, the diastolic pressure in the veins must be high (otherwise the neck veins would collapse and be visible in lower positions). The mean atrial and central venous pressure of these patients is probably high.

II. CLINICAL SIGNIFICANCE

A. DETECTING TRICUSPID REGURGITATION

The presence of the characteristic systolic murmur of tricuspid regurgitation increases the probability of tricuspid regurgitation (LR = 14.6; see Chapter 43). However, many patients with tricuspid regurgitation lack a murmur, which means that the *absence* of a murmur has less diagnostic significance (i.e., negative LRs are either not significant or close to the value of 1; see Chapter 43).

B. SEVERITY OF TRICUSPID REGURGITATION

From palpation of the precordium or inspection of neck veins alone, the diagnosis of moderate-to-severe tricuspid regurgitation may be obvious (see EBM Box 46.1). Diagnostic findings include the RV rock (LR = 31.4), lower sternal pulsations (LR = 12.5), early systolic outward venous pulsation (i.e., the CV wave, LR = 10.9; see Chapter 36), and hepatic pulsations (LR = 6.5). The absence of any of these findings, however, is diagnostically unhelpful.

PULMONIC REGURGITATION

I. THE FINDING

The murmur of pulmonic regurgitation is a diastolic murmur heard best at the second left intercostal space. Its timing and frequency depend on pulmonary pressures.

A. HIGH-PRESSURE PULMONIC REGURGITATION

Sustained pulmonary hypertension may cause the pulmonic valve to become incompetent, producing an early diastolic, high-frequency murmur at the second left intercostal space. The murmur begins immediately after a loud S_2, and most patients have elevated neck veins and other auscultatory findings of pulmonary hypertension, such as the pulmonary ejection sound, abnormal S_2 splitting, and right ventricular gallops (see Chapters 40 to 42).[40] Chapter 45 discusses how to distinguish this murmur from that of aortic regurgitation.

The high-pressure pulmonic regurgitation murmur was first described by the British clinician Graham Steell in 1888[41] and is often called the **Graham Steell murmur**.

B. LOW-PRESSURE PULMONIC REGURGITATION

When pulmonary pressures are normal, pulmonic regurgitation represents primary valvular disease (e.g., endocarditis). This murmur is mid-diastolic and contains a mixture of low- and high-frequency sound. It begins with a short delay after S_2.[39]

II. CLINICAL SIGNIFICANCE

A. DETECTING PULMONIC REGURGITATION

Although the presence of the characteristic murmur is diagnostic (LR = 17.4; see Chapter 43), the absence of the murmur is unhelpful (LR not significant, see Chapter 43).

B. DETECTING PULMONARY HYPERTENSION

In patients with mitral stenosis, the presence of the high-pressure pulmonary regurgitation murmur (i.e., Graham Steell murmur) increases probability of pulmonary hypertension (mean pulmonary artery pressure ≥50 mm Hg; LR = 4.2; EBM Box 46.2).

C. HEMODIALYSIS PATIENTS

A common cause of an early diastolic murmur at the sternal border in patients with end-stage renal disease is pulmonic regurgitation.[43] This murmur presumably occurs

from volume overload because it is loudest immediately before dialysis and often disappears just after dialysis.

MITRAL STENOSIS

I. THE FINDINGS

A. THE MURMUR

Mitral stenosis causes a low-frequency, rumbling mid-diastolic murmur, which is usually heard with the bell lightly applied to the apex, often only after the patient has turned to the left lateral decubitus position. The murmur peaks during mid-diastole and again immediately before the first heart sound (**presystolic accentuation**). The mid-diastolic peak occurs because the mitral leaflets move backward toward the left atrium at this time, narrowing the mitral orifice and causing more turbulence (an analogy is the difficulty whistling with the mouth open).[44,45] The importance of these movements to the sound may explain why some patients with severe calcific mitral stenosis and inflexible leaflets lack murmurs.[45]

The traditional explanation for presystolic accentuation is atrial systole, but this is probably incorrect because presystolic accentuation also occurs in patients with atrial fibrillation.[46] Instead, there is some evidence that presystolic accentuation is actually caused by *ventricular* contraction: the crescendo sound occurs because the closing movement of the mitral leaflets, induced by ventricular systole, occurs when a pressure gradient is still maintaining forward flow across the valve. The sound continues and crescendos up until the moment the valves completely close, at the first heart sound (therefore the "presystolic" accentuation is not presystolic at all but instead is systolic).[44-46]

Because the sound vibrations of mitral stenosis border on the threshold of human hearing, this murmur is indistinct and the most difficult to detect, as reflected in similes used to describe the sound: "the faint sound of distant thunder," "the rumbling sound of a ball rolling down a bowling alley," and "the absence of silence."[47]

B. OTHER CARDIAC FINDINGS

Other cardiac findings in mitral stenosis include an irregular pulse (atrial fibrillation), loud first heart sound, opening snap (early diastolic sound), and associated findings of pulmonary hypertension, including elevated neck veins with an exaggerated A wave, right ventricular parasternal impulse, and a palpable P_2 (see Chapters 36, 38, and 40).[9] The palpable apical impulse is small or absent because of obstruction of blood flow into the left ventricle.[9]

II. CLINICAL SIGNIFICANCE

A. THE MURMUR

Mitral stenosis has become a rare diagnosis in developed countries, where the characteristic apical diastolic rumble instead may reflect another disorder, such as mitral annular calcification, Austin Flint murmur, atrial myxoma, or flow rumbles (i.e.,

EBM BOX 46.2
*Other Cardiac Findings in Mitral Stenosis**

Finding (Reference)†	*Sensitivity (%)*	*Specificity (%)*	*Likelihood Ratio‡ if Finding is*	
			Present	*Absent*
Graham Steell Murmur				
Detecting pulmonary hypertension[42]	69	83	**4.2**	0.4
Hyperkinetic Apical Movement				
Detecting associated mitral regurgitation or aortic valve disease[9]	74	93	**11.2**	**0.3**
Hyperkinetic Arterial Pulse				
Detecting associated mitral regurgitation[9]	71	95	**14.2**	**0.3**

*Diagnostic standard: for *pulmonary hypertension*, mean pulmonary pressure greater than 50 mm Hg.[42]

†Definition of findings: for *Graham Steell murmur*, early diastolic decrescendo murmur of high-pressure pulmonic regurgitation at second left intercostal space; for *hyperkinetic apical movement*, apical "thrust" [9] (see Chapter 38); for *hyperkinetic pulse*, arterial pulse strikes fingers abruptly and strongly (see Chapter 15).

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, Not significant.

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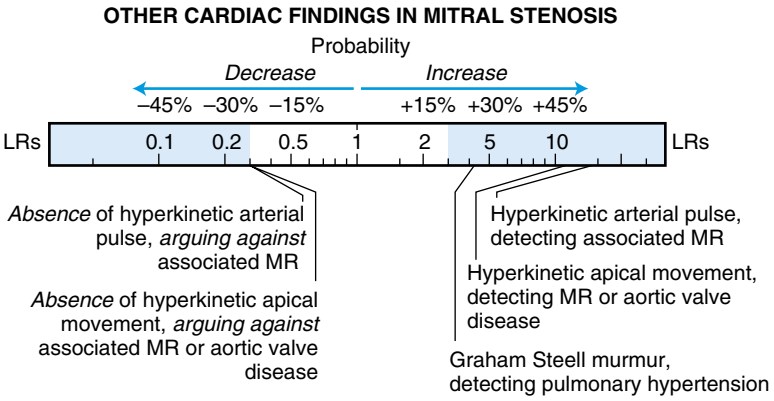

increased flow over a nonobstructed mitral valve from mitral regurgitation, ventricular septal defect, or high-output states; see Chapter 41). In one study of 529 elderly patients living in the United States, an apical diastolic rumble detected *mitral annular calcification* on echocardiography with a sensitivity of 10%, specificity of 99%, and positive LR = 7.5 (90% of patients with this murmur had *no* mitral stenosis).[48]

B. OTHER CARDIAC FINDINGS

In patients with mitral stenosis, the apical impulse should be absent or small and the arterial pulse should be normal or reduced. Consequently, the finding of a hyperkinetic apical movement in patients with mitral stenosis suggests additional mitral or aortic regurgitation (LR = 11.2; see EBM Box 46.2), and the finding of a hyperkinetic arterial pulse strongly suggests additional mitral regurgitation (LR = 14.2; see EBM Box 46.2).

ARTERIOVENOUS FISTULAE: THE HEMODIALYSIS FISTULA

The hemodialysis fistula provides a good example of the continuous murmur typical of arteriovenous fistulae: it is a high-frequency murmur, persisting throughout systole and diastole, and peaking during late systole:

PushshSHSH**Pu**SHshshshshshshsh

Moving the stethoscope progressively away from the fistula and toward the heart makes the diastolic component of the murmur fainter until only a systolic murmur remains.[49]

The importance of this murmur is that its systolic remnants are transmitted to the upper sternal border, where they can be mistaken for cardiac murmurs, unless the clinician traces them to the fistula (see "Isolated Base" murmur pattern in Fig. 43.1).[15,49]

In contrast to murmurs from arteriovenous fistulas, continuous murmurs generated from abnormal flow in veins (e.g., venous hums, mammary souffle) peak during diastole (see Chapter 43).

The references for this chapter can be found on www.expertconsult.com.

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